Dengue Epidemiology in the United States and U.S. Territories: Perspective as a Vaccine Preventable Disease

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Outline – Dengue in U.S. Territories

I Dengue Epidemiology Background

II Puerto Rico

II Other US Territories

III US Mexico Border Region

IV Florida

V Hawaii

VI Summary
Dengue Viruses (DENV)

- Long-term protection to infecting virus-type
- No long-term cross protective immunity
- Can be infected up to 4 times during lifetime
DENV: Humans the Primary Host

Mosquito acquires virus during feeding, virus replicates in mosquito

Mosquito infects susceptible person

Mosquito acquires virus during feeding, virus replicates in mosquito

Mosquito infects humans – virus in lymph nodes, other organs, blood
### Dengue is a Global Problem

![Map of global distribution of Dengue](image)

- **Evidence Consensus**
  - **Absent**
  - **Present**

### Epidemiological Data

<table>
<thead>
<tr>
<th>Region</th>
<th>Dengue Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>13 (10-19)</td>
</tr>
<tr>
<td>Europe</td>
<td>16.0 (11-23)</td>
</tr>
<tr>
<td>Africa</td>
<td>67 (47-94)</td>
</tr>
<tr>
<td>Latin America</td>
<td>41 (31-53)</td>
</tr>
<tr>
<td>North America</td>
<td>100 million</td>
</tr>
<tr>
<td>South America</td>
<td>204 (152-273)</td>
</tr>
<tr>
<td>Middle East</td>
<td>0.2 (0.1-0.3)</td>
</tr>
<tr>
<td>Australia</td>
<td>0.6 (0.4-0.8)</td>
</tr>
<tr>
<td>Africa</td>
<td>100 million</td>
</tr>
<tr>
<td>South America</td>
<td>300 million</td>
</tr>
</tbody>
</table>

**Adapted from Bhatt, S et al. Nature 2013; 496: 504-507**
Dengue is an acute febrile illness (AFI) syndrome

Incidence: high endemic + cyclical epidemics

Highly seasonal

Often several circulating DENV types

Peak age of incidence may vary by region

Severe dengue is natural progression of disease
Risk factors for severe dengue

- Secondary infections
- Virus strain
- Host genetics
- Co-morbidities
- Young age
- Female
Dengue in the United States
A Risk-Assessment Framework

• **Vector present** – endemic dengue
  – Caribbean: Puerto Rico, Virgin Islands
  – Pacific Islands

• **Vector present** – non-endemic – potential for transmission
  – Outbreaks in: Texas (US - Mexico border), Florida, Hawaii
  – Many states (e.g., FL, GA, AL, LA, MI, SC, NC, TX, AZ, CA)

• **Vector not present**
**History of Dengue in Puerto Rico**

- First major epidemics reported in 1915 and 1945
- In 1963, DENV first isolated in Puerto Rico
- First laboratory confirmed case of dengue hemorrhagic fever (DHF) reported in 1975
- First time more than one DENV type in circulation was in 1977 outbreak
  - DENV- 1, 2 and 3 were detected
- During 1969–1986, there were six large, island-wide outbreaks
Current Epidemiology of Dengue in Puerto Rico

- Only *Ae. aegypti* present
- **Endemic**
  - 1960s–2013*: ~3,000–27,000 suspected cases per year
  - 3–4 DENVs co-circulating since 1980s
- **Seasonal**
  - Low incidence in Dec–Mar
  - High incidence in July–Sept
- **Geospatial clustering**
  - Higher population density = higher incidence
- **Burden of disease highest among 10–19 year-olds**
  - No difference by sex

*Chikungunya and Zika viruses first detected in May 2014 and November 2015, respectively.*
‘Suspect Dengue’ in Puerto Rico 1986-2013
Percent of Dengue Virus Isolates by Type and Year — Puerto Rico, 1986–2012
Age Distribution of Laboratory Positive Dengue Cases — Puerto Rico, 2010–2012

49% of lab positive cases were adults
Median age: 18 years. Range: 1 mo. – 102 years
Laboratory Positive Dengue Cases and Fatal Cases by Month of Illness Onset, 2010–2012, Puerto Rico

<table>
<thead>
<tr>
<th>Month</th>
<th>Fatal Laboratory Positive Dengue Cases</th>
<th>All Laboratory Positive Dengue Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan-10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mar-10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>May-10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jul-10</td>
<td>2500</td>
<td>2000</td>
</tr>
<tr>
<td>Sep-10</td>
<td>1500</td>
<td>1000</td>
</tr>
<tr>
<td>Nov-10</td>
<td>1000</td>
<td>500</td>
</tr>
<tr>
<td>Jan-11</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mar-11</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>May-11</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jul-11</td>
<td>1000</td>
<td>500</td>
</tr>
<tr>
<td>Sep-11</td>
<td>500</td>
<td>250</td>
</tr>
<tr>
<td>Nov-11</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jan-12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mar-12</td>
<td>0</td>
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<tr>
<td>May-12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jul-12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sep-12</td>
<td>500</td>
<td>250</td>
</tr>
<tr>
<td>Nov-12</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

39 deaths 1.05 deaths per 100,000
6 deaths 0.16 deaths per 100,000
13 deaths 0.35 deaths per 100,000

Age Distribution of Fatal Laboratory-Positive Dengue Cases — Puerto Rico, 2010–2012

90% of deaths were in adults
Median age: 46 years. Range: 6 mo. – 88 years

No. Fatal Laboratory Positive Dengue Cases
Seroprevalence of DENV infection and proportion of primary vs. secondary infections

- **2006**: serosurvey among blood donors (only adults)\(^1\)
  - \(~92\%\) seropositive
    - \(~96\%\) secondary infections

- **2010**: among lab-positive dengue cases\(^2\)
  - \(~80\%\) of all infections were secondary
  - Primary infection more common only among 1–4 year-olds
  - \(>80\%\) of all adults had secondary infection

\(^1\)Mohammed et al., Transfusion, 2012
Dengue in US Virgin Islands

- **US Virgin Islands**
  - St. Croix, St. John, St. Thomas and Water Island
  - *Aedes aegypti* present throughout
  - Passive case reporting

- **Periodic outbreaks**
  - 1986-1987 (DENV-2, -4), St. Johns
  - 1990 (DENV-1, -2, and -4), all islands
  - 2004 (DENV-2), St. Thomas
  - 2005 (DENV-2), St. Croix
  - 2012 (DENV-1, -4), St. Croix
    - School survey: ~20% acute/recent infections
Dengue in the US-affiliated Pacific Islands† and Territories*

- *Ae. albopictus* and *aegypti* both present, as well as less common vectors (e.g., *Ae. hensilii*, *Ae. marshallensis*)
- Periodic outbreaks detected since 1958 (Guam¹)
  - Unclear which, if any, are endemic
- Often only one DENV type circulating at a time
- 2010 serosurvey in American Samoa (adults only): 96% seropositive²

*American Samoa, Guam, Northern Mariana Islands; †Palau, Republic of the Marshall Islands, Federated States of Micronesia
²Lau, EID, 2013.
Dengue Outbreak in American Samoa, 2015

- **May–November: 479 suspected dengue cases**
  - ~1% of population
- **Incidence highest among individuals aged <25 years**
- **Only DENV detected by RT-PCR was DENV-3**
- **4 fatal cases**
  - CFR = ~1%
- **Most common vectors were Ae. polynesiensis and aegypti**
Dengue in the U.S. – Mexico Border Region
Locally-acquired Dengue in Texas

- **Historical outbreaks**
  - First outbreak 1885-86: >70% of Austin residents affected
  - Last 1922: ~500,000 cases throughout the state

1Ehrenkranz et al., NEJM 1971.
Locally-acquired Dengue in South Texas

- 3 outbreaks prior to 1999
  - 1980: 28 cases in Brownsville and nearby Texas border towns; DENV-1
  - 1986: 9 cases, Brownsville (4), Corpus Christi (3), Laredo (2); DENV-1
  - 1995-6: 7 cases Brownsville (3), McAllen (4): DENV-2, 4

MMWR 45(39) 1996
Dengue in Laredo, Texas /Nuevo Laredo, Tamaulipas, Mexico, 1999

- **Seroprevalence**
  - Mexico (n=288)
    - IgM – 16.0%
    - IgG – 47.8%
  - U.S. (n=228)
    - IgM – 1.3%
    - IgG – 22.5%

- **Evidence of local transmission**

- **Lack of air conditioning a risk factor for dengue infection**

Reiter et al. *Emerging Infectious Diseases* 2003
Seroprevalence
- Mexico (n=132)
  - IgM – 22.8%
  - IgG – 76.6%
- U.S. (n=141)
  - IgM – 2.5% (0-5.4, 95% CI)
  - IgG – 38.2% (26.7-49.8, 95% CI)

DENV-2, SE Asia strain

Clinical classification
- Mexico – > 6800 cases, > 50% hospitalized, estimate 1/3 with DHF
- U.S. – 25/28 (89%) hospitalized; 16 DHF cases

Evidence of local transmission
Dengue in Cameron County, 2013

- DENV-1, 3
- 53 laboratory positive cases from enhanced surveillance
- 55% hospitalized
- 49% locally acquired
- Cluster survey – 6 (12%) of 51 household members of dengue cases with recent dengue and no travel

Thomas et al. Emerg Inf Dis 2016
Locally-acquired Dengue in Florida, 2009-2010

- 27 cases in Monroe County (Key West) in 2009
  - DENV-1
  - 2009 Onset: July 19–Oct 18, 2009

- Serosurvey in Key West Sept 2009
  - 5% had acute/recent dengue

- 66 cases in Monroe County in 2010
  - 2010 Onset: March 20–Nov 30, 2010

Data: Florida Department of Health
Locally-acquired Dengue in Florida, 2010-2012

- **2 sporadic cases in 2010**
  - Miami-Dade (1) and Broward (1) counties

- **7 sporadic cases in 2011**
  - Miami-Dade (3), Palm Beach (2) Hillsborough (1), and Martin (1) counties

- **4 sporadic cases in 2012**
  - Miami-Dade (2), Seminole (1) and Osceola (1) counties
Locally-acquired Dengue in Florida, 2013

- **21 cases Martin/St Lucie county**
  - All DENV-1
  - Onset: June 16 – present
  - Median age: 48 years (range: 4 to 63)
  - 57% male and >85% non-Hispanics

- **1 case in Miami-Dade county**
  - DENV-4

![Martin County Dengue Outbreak](image)

Data: Florida Department of Health
Locally-acquired Dengue in Florida, 2013

- Sequence analysis done at CDC-DB
  - Is this Key West DENV-1 strain? No

Key West (Monroe County) 2009-2010

Martin/St. Lucie County 2013

Data: CDC Dengue Branch and Florida Department of Health
Locally-acquired Dengue in Hawaii

- **Historical outbreaks**
  - First outbreak in late 1840s
  - 1903
  - 1943-44, Oahu
    - DEN1
    - 1500 cases
  - Aedes aegypti introduced first
  - Aedes albopictus introduced in early 20th century

Locally-acquired Dengue in Hawaii, 2001

- **2001 outbreak**
  - Maui, Oahu, Kauai
  - 1644 suspected cases; 122 positive
  - 39% attack rate, Nahiku, Maui
  - DENV-1 genotype IV Tahitian strain
  - Median age: 41 years (range 1—77)
  - Three hospitalized; no DHF/DSS cases
  - *Aedes albopictus*
Locally-acquired Dengue in Hawaii, 2011

- 2011 outbreak in Oahu
  - January – March 2011
  - 5 laboratory positive cases
  - DENV-1
  - Index case: traveler from Philippines
  - All cases from same neighborhood
  - No DHF/DSS cases or deaths
Locally acquired Dengue in Hawaii, 2015-16

- 2015-2016 outbreak on Island of Hawaii (Big Island)
  - 264 lab confirmed infections
  - Median age: 29 years (range 0-80)
  - 14% hospitalized
  - DENV-1, Asian strain
  - Predominantly *Aedes albopictus*

MMWR 2016 65(2): 34-35
Summary

- Dengue is highly endemic in Puerto Rico with simultaneous circulation of multiple serotypes
  - Limited seroprevalence data strongly suggests most of population has had at least one dengue infection by the second decade of life
  - During large outbreaks 100’s of hospitalizations and tens of deaths occur

- Dengue is common and may be endemic in the Virgin Islands and American Samoa and other US Pacific territories
  - Seroprevalence data limited
Summary

- South Texas with repeated small dengue outbreaks and local transmission since the 1980s
  - Seroprevalence data > 10 years old suggests border crossing sub-population with significant past exposure to dengue
- Other US –Mexico border states at risk for dengue but no evidence of local transmission to date
- South Florida - repeated small dengue outbreaks since 2009
- Hawaii has had two outbreaks and a small cluster of cases since 2001
  - Primarily *Aedes albopictus* transmitted
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